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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,775	10/06/2003	Lieping Chen	07039-442001	5247

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EXAMINER	
OUSPENSKI, ILIA I	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/679,775	CHEN, LIEPING	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2007 and 10 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-14 and 31-50* is/are pending in the application.

4a) Of the above claim(s) *31-41 and 44-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,42 and 43* is/are rejected.

7)☒ Claim(s) *5-14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed on 01/23/2007 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/23/2007 has been entered.

2. Applicant's amendment/remarks, filed on 11/10/2007, are acknowledged, and have been entered.

Claims 1 – 2, 4 – 14, and 31 – 50 are pending.

Claims 31 – 41 and 44 – 50 have been withdrawn from consideration by the Examiner as being drawn to nonelected inventions (see Office Action mailed 03/21/2006).

Claims 1 – 2, 4 – 14, and 42 – 43 are under consideration in the instant application.

3. Applicant's arguments regarding the withdrawn embodiments of variants of "human B7-H1" are acknowledged. In the interest of compact prosecution, the examination has been extended to include the embodiment of variants of human B7-H1.

4. This Office Action will be in response to applicant's amendment and arguments, filed 11/10/2006.

The rejections of record can be found in the previous Office Action, mailed 09/26/2006.

It is noted that New Grounds of Rejection are set forth herein.

5. The objections and rejections of record have been withdrawn in view of Applicant's amendment and arguments, except as set forth herein.

6. The following is a quotation of the **first paragraph of 35 U.S.C. 112**:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 2, and 4 are rejected under **35 U.S.C. 112, first paragraph**, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims recite a genus of polypeptides defined as "variants" of a reference sequence, and a requirement that the variant polypeptides have a reduced binding affinity for PD-1. Applicant has disclosed only a limited number of such "variants". In the absence of a structural basis for that function that must be maintained by the members of the genus, the claimed invention is not described in such a way as to

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

Further, even single amino acid differences can result in drastically altered functions between two costimulatory proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus it is unpredictable if the required functional activity will be shared by "variants" other than those having the specifically disclosed amino acid substitutions.

In view of this unpredictability, the skilled artisan would not reasonably expect a generically recited "variants" to possess the required functions, and there is insufficient guidance to direct the skilled artisan as to such functional sequences. Thus the instant claim language does not allow the skilled artisan to make and use the variant polypeptides commensurate in scope with the instant claims without undue experimentation.

8. Claims 42 and 43 stand rejected under **35 U.S.C. 112, first paragraph**, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

It is maintained, for the reasons of record, that in the absence of a limitation specifying a minimal size of the recited "fragments," the specification does not provide a sufficient enabling description of polypeptide fragments comprising the specified amino acids of SEQ ID NO:4, wherein the fragments inhibit binding of murine B7-H1 to murine PD-1.

Applicant's arguments have been fully considered but have not been found convincing.

Applicant's argument is essentially the same as of record. Applicant argues that given the disclosure of the methods of testing the ability of a polypeptide fragment to bind PG-1, and the high level of skill in the art, no undue experimentation would be required to make the recited fragments.

In response, it is maintained that since the only structural requirements for the claimed fragments are that they comprise tripeptides of amino acids 67 – 69 or 113 – 115, one of skill in the art is faced with a daunting task of testing a vast number of fragments of various sizes and sequences. In view of the unpredictability of the art, as addressed in the previous Office Actions, such experimentation is unnecessarily, and improperly, extensive and undue. In the absence of a limitation specifying a minimal size of the recited "fragments," the specification does not provide a sufficient enabling description of the claimed invention.

Therefore, the rejection of record is maintained for the reasons of record, as it applies to the amended claims. The rejection or record is incorporated by reference herein, as if reiterated in full.

9. Applicant's request for rejoinder of claims 35 – 41 and 44 – 50 is acknowledged. Since the elected claims directed to a product have not been found allowable, the withdrawn process claims are not presently considered for rejoinder.

10. Claims 5 – 14 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ILIA OUSPENSKI, Ph.D.
Patent Examiner
Art Unit 1644

April 10, 2007

PHILLIP GAMBEL, PH.D. JD
PRIMARY EXAMINER
TC 1600
4/11/07